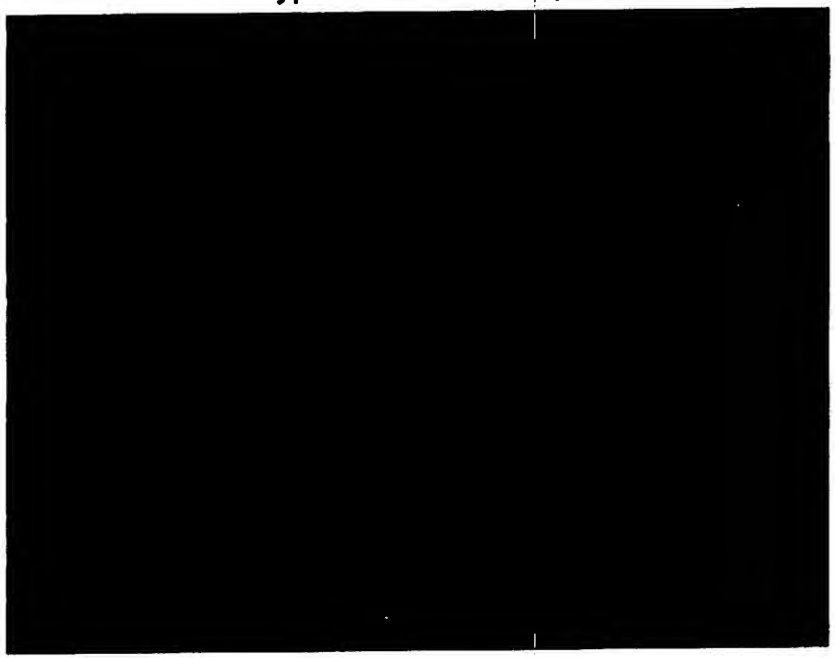
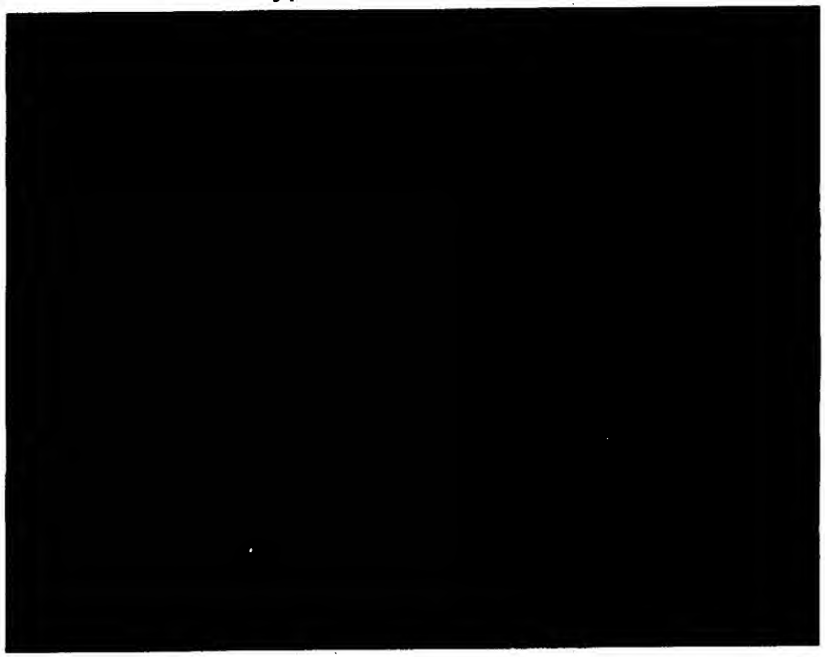
Immunostaining of alpha 1C subunit in the wild type HEK 293 cells and cells stably transfected with the L-type Δ1C channel (C1-6-37-3)



C1-6-37-3 cells

FIG.1A

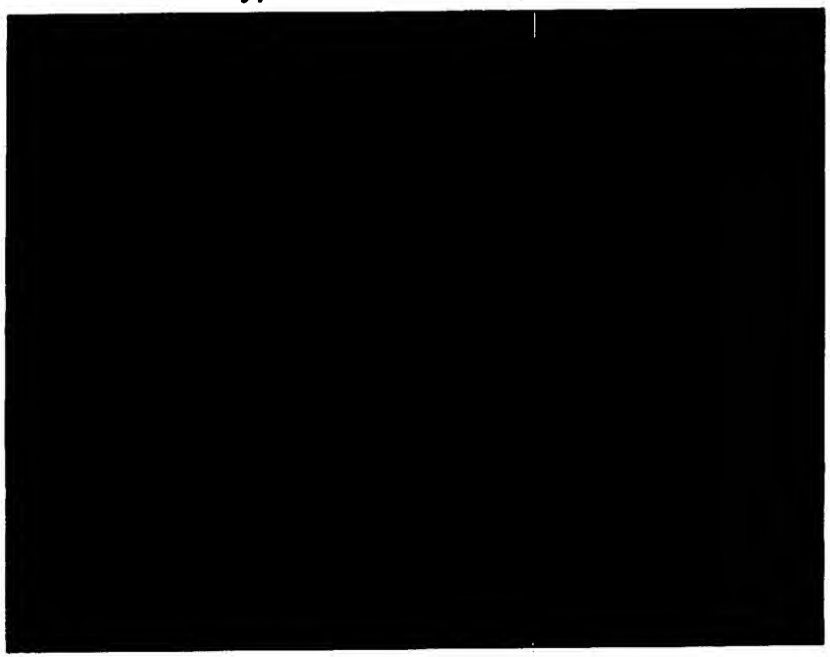
Immunostaining of alpha 1C subunit in the wild type HEK 293 cells and cells stably transfected with the L-type Δ1C channel (C1-6-37-3)



Wild type HEK 293 cells

FIG.1B

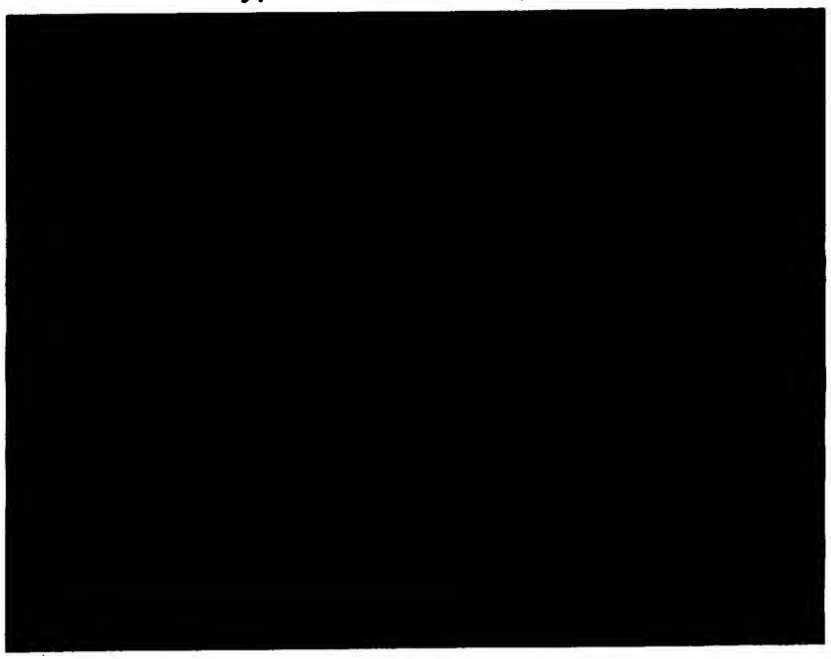
Immunostaining of Kir2.3 subunit in the wild type HEK 293 cells and the cells stably transfected with the L-type Δ1C channel (C1-6-37-3)



C1-6-37-3

FIG.2A

Immunostaining of Kir2.3 subunit in the wild type HEK 293 cells and the cells stably transfected with the L-type Δ1C channel (C1-6-37-3)



Wild type HEK 293

FIG.2B

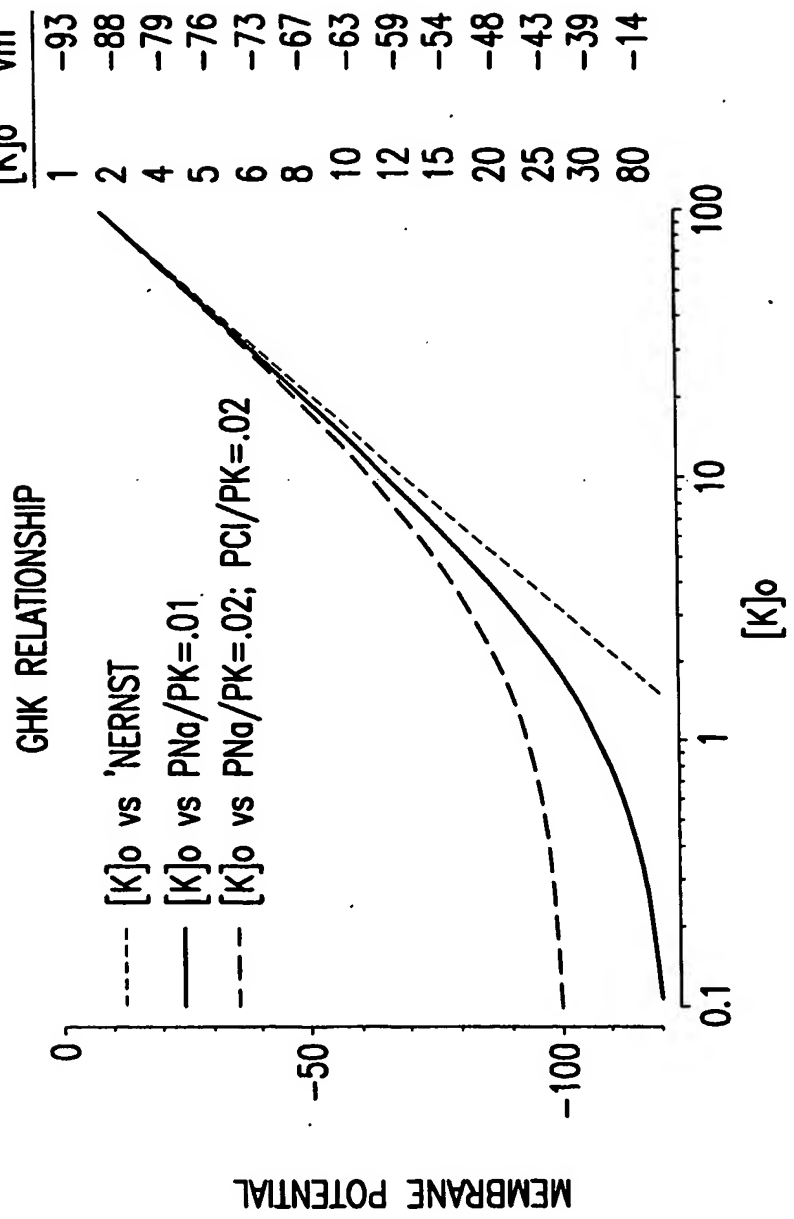

GHK RELATIONSHIP
[K]o vs 'NERNST
[K]o vs PNa/PK=.01
[K]o vs PNa/PK=.02; PCl/PK=.02
MEMBRANE POTENTIAL
0
-50
-100
0.1
1
10
100
[K]o
[K]o Vm
1 -93
2 -88
4 -79
5 -76
6 -73
8 -67
10 -63
12 -59
15 -54
20 -48
25 -43
30 -39
80 -14

FIG.3

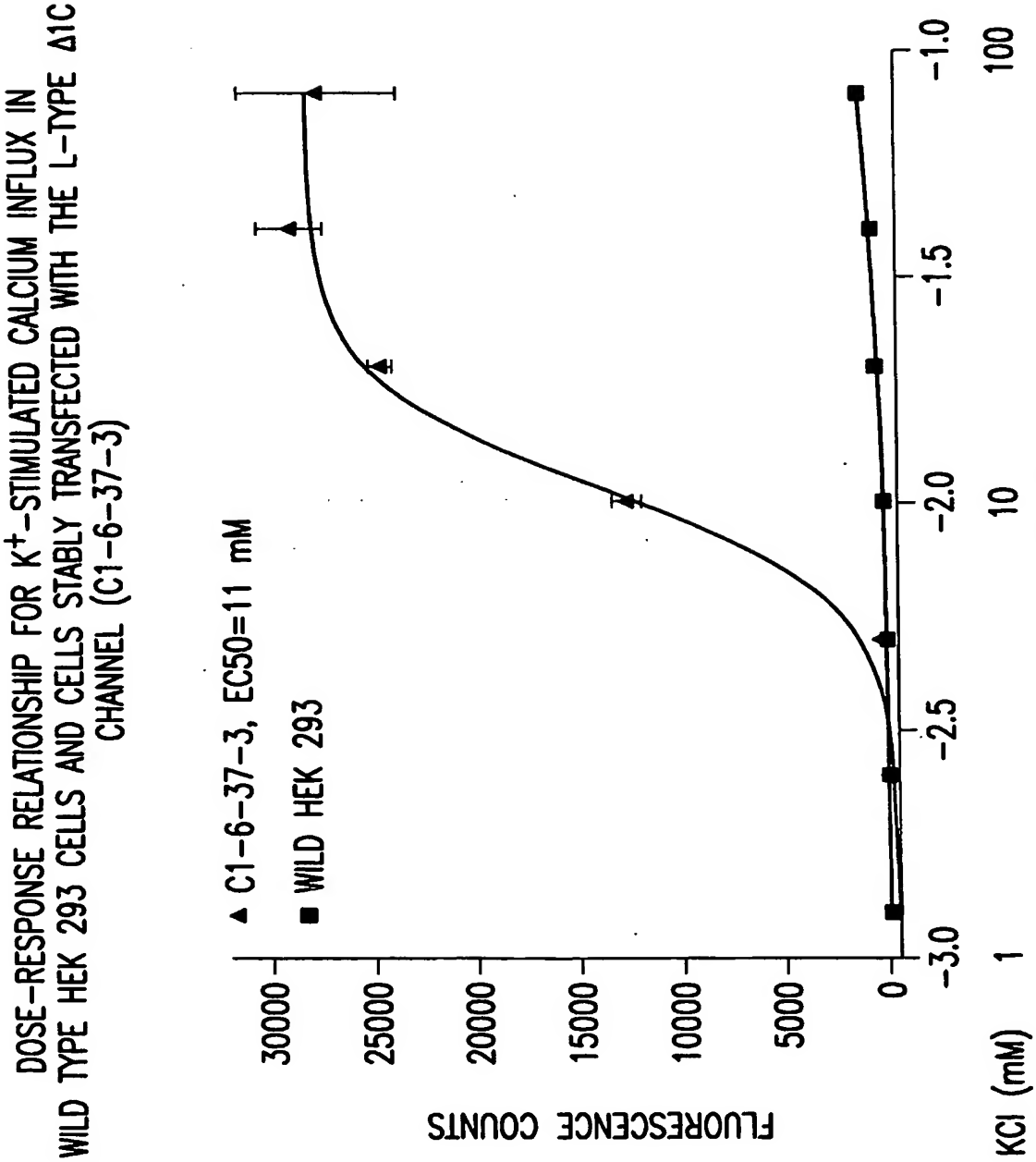

DOSE-RESPONSE RELATIONSHIP FOR K+-STIMULATED CALCIUM INFLUX IN WILD TYPE HEK 293 CELLS AND CELLS STABLY TRANSFECTED WITH THE L-TYPE Δ1C CHANNEL (C1-6-37-3)
▲ C1-6-37-3, EC50=11 mM
■ WILD HEK 293
FLUORESCENCE COUNTS
30000
25000
20000
15000
10000
5000
0
-3.0
-2.5
-2.0
-1.5
-1.0
1
10
100
KCl (mM)

FIG.4

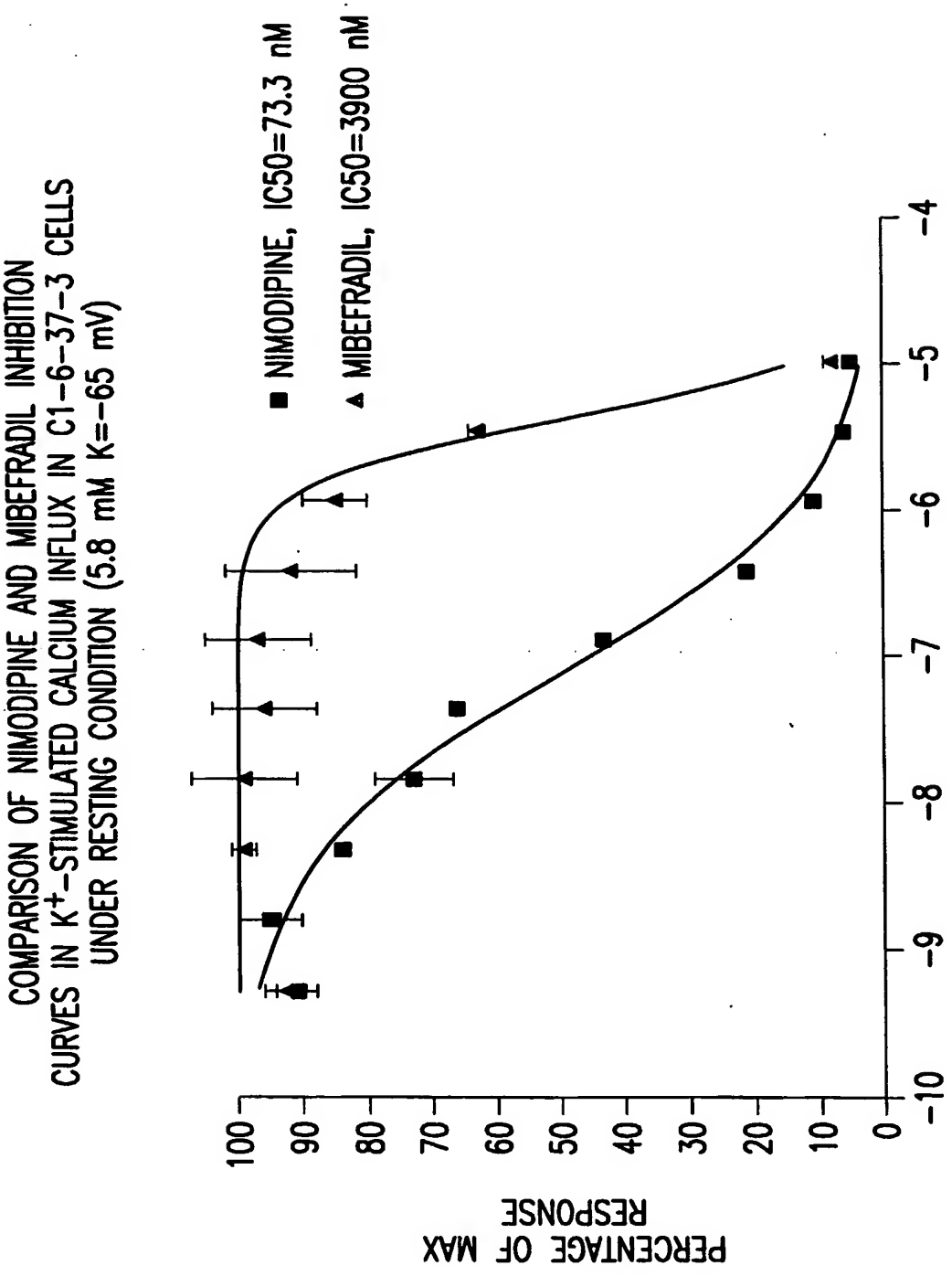

COMPARISON OF NIMODIPINE AND MIBEFRADIL INHIBITION
CURVES IN K+-STIMULATED CALCIUM INFLUX IN C1-6-37-3 CELLS
UNDER RESTING CONDITION (5.8 mM K=-65 mV)
■ NIMODIPINE, IC50=73.3 nM
▲ MIBEFRADIL, IC50=3900 nM
PERCENTAGE OF MAX RESPONSE
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
ANTAGONISTS (M)

FIG.5

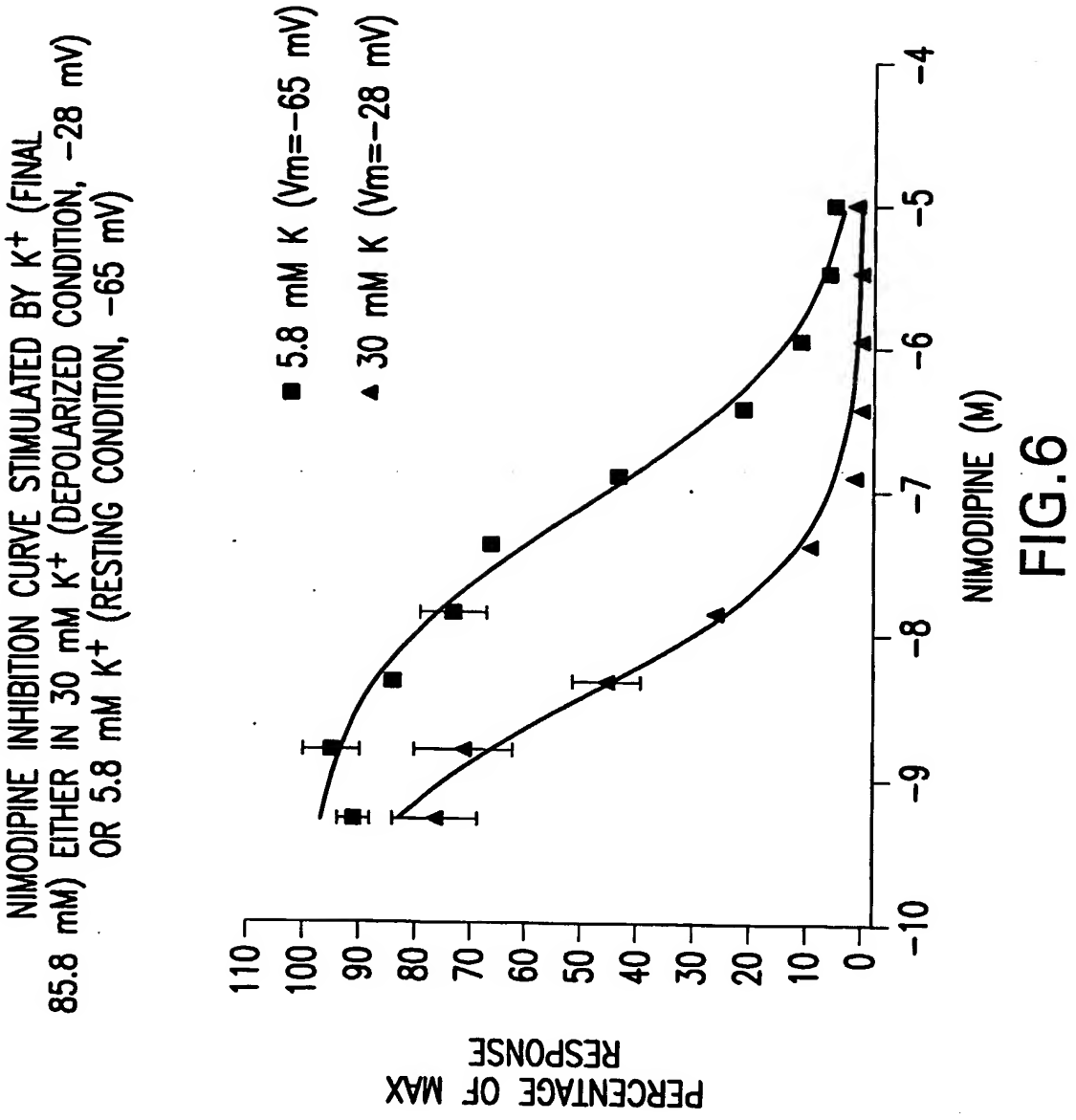

NIMODIPINE INHIBITION CURVE STIMULATED BY K+ (FINAL 85.8 mM) EITHER IN 30 mM K+ (DEPOLARIZED CONDITION, −28 mV) OR 5.8 mM K+ (RESTING CONDITION, −65 mV)
■ 5.8 mM K (Vm=−65 mV)
▲ 30 mM K (Vm=−28 mV)
PERCENTAGE OF MAX RESPONSE
110
100
90
80
70
60
50
40
30
20
10
0
−10
−9
−8
−7
−6
−5
−4
NIMODIPINE (M)

FIG.6

IC50 (nM) VALUES OF CLACIUM CHANNEL BLOCKERS FOR INHIBITION OF K^+-INDUCED CALCIUM INFLUX EITHER IN 30 mM K^+ (DEPOLARIZED CONDITION) OR 5.8 mM K^+ (RESTING CONDITION)

COMPOUNDS	5.8 mM [K]o	n	30 mM [K]o	n	F
NIMODIPINE	59 ρ 27	4	3 ρ 3	5	20
VERAPAMIL	16220 ρ 1395	2	695 ρ 41	4	23
DILTIAZEM	16020 ρ 523	2	1888 ρ 155	3	8
AMLODIPINE	2980 ρ 747	7	390 ρ 164	2	8
NIFEDIPINE	43 ρ 12	4	7 ρ 1	3	6
NITRENDIPINE	51 ρ 18	4	6 ρ 3	2	9
NICARDIPINE	160 ρ 30	2	13 ρ 1	2	12
LERCANIDIPINE	509 ρ 48	2	14 ρ 5	2	36
EFONIDIPINE	1821 ρ 693	2	68 ρ 25	2	28
LACIDIPINE	116 ρ 19	2	10 ρ 8	2	12
MIBEFRADIL	3458 ρ 867	4	791 ρ 43	5	4

FIG.7

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